Citation:

Innis SM, Gilley J, Werker J. Are human milk long-chain polyunsaturated fatty acids related to visual and neural development in breast-fed term infants? *J Pediatr.* 2001 Oct;139(4):532-8.

PubMed ID: 11598600

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine whether docosahexaenoic acid (DHA) is related to visual and neural development in term breast-fed infants.

Inclusion Criteria:

- Term birth
- Birthweight 2500-4500 grams
- Enrolled within 2 weeks of birth
- Maternal intent to exclusively breastfeed ≥ 3 months
- No solid foods ≥ 4 months

Exclusion Criteria:

- Maternal substance abuse
- Communicable diseases, metabolic or physiologic problems (unspecified)
- Infections likely to influence fetal growth
- Multiple births
- Infants with metabolic or physical abnormalities (unspecified)

Description of Study Protocol:

Recruitment : Method of recruitment not described.

Design Prospective cohort study

Blinding used (if applicable): not applicable

Intervention (if applicable): exposure to exclusive breastfeeding for 3 months

Statistical Analysis:

- Multiple linear regression analysis to determine impact of fatty acid variables on growth, vision, neurodevelopmental outcome (on language acquisition test).
- Data was controlled for duration of breastfeeding, maternal education and smoking, infant birth measures (weight, length, head circumference).
- Statistical test of correlation was Pearson's correlation coefficient and associated p-values were reported.

Data Collection Summary:

Timing of Measurements:

- Blood and breast milk sampled at 2 months
- Visual acuity measures : Teller Acuity Cards at 2, 4, 6, and 12 months
- Speech perception by conditioned head-turn procedure at 9 months
- Growth measures at 1, 2, 4, 6, 9, and 12 months
- Novelty Preference test using the Fagan Test of infant Intelligence at 6 and 9 months
- Bayley's MDI and PDI at 6 and 12 months
- Object Search task (age not specified)

Dependent Variables

- Infant and maternal breastmilk, red blood cell, and plasma fatty acids
- Visual acuity
- Speech perception
- Object search task
- Bayley's Mental Development Index and Psychomotor Development Index
- Novelty Preference test

Independent Variables

- DHA in breastmilk for 3 months

Control Variables

- Duration of breastfeeding
- Maternal education and smoking
- Infant birth measures

Description of Actual Data Sample:

Initial N: 83 infants enrolled : 39 male and 44 female

Attrition (final N): 75 infants exclusively breastfed $\geq$ 3 months. Outcome measures not obtained on all infants at each measurement point.

Age: not reported, infants enrolled at 2 weeks of age

Ethnicity: not reported

Other relevant demographics:

Anthropometrics

Location: Canada

Summary of Results:

Key Findings

- The infant red blood cell phosphatidylethanolamine DHA was significantly related to visual acuity at 2 months of age (r = 0.32, P = 0.01) and 12 months of age (r = 0.30, P = 0.03).
- The ability to discriminate nonnative retroflex and phonetic contrasts at 9 months of age was related to the plasma phospholipid DHA (r = 0.48, P < 0.02) and red blood cell phosphatidylethanolamine DHA (r = 0.26, P = 0.02) at 2 months of age after adjusting for covariates.

Author Conclusion:

DHA may influence the development of visual acuity and neural pathways associated with the developmental progression of language acquisition in term breast-fed infants. The extent to which our results can be attributed solely to DHA from maternal sources through breast milk or in gestation or other confounding factors remains to be determined.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes

1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A

4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes

7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes